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THE ROCKEFELLER UNIVERSITY
1230 YORK AVENUE · NEW YORK, NEW YORK 10021

25 June 1980

Dr. Joshua Lederberg
President

Dear Dr. Lederberg:

S.A. Narang is one of four or five synthetic nucleotide chemists who worked with Khorana in the 60's when he was at Madison. At that time I was more familiar with Hayatsu because he was trying to use solid phase methodology on oligonucleotides. The others, including Narang, were using solution methods, which I did not study in any detail even though they turned out to be more successful.

The fact that I don't know Narang does not, of course, reflect at all on his elegant work. The Khorana group accomplished a large amount of quite difficult synthetic chemistry and applied column chromatography to obtain pure samples of many di, tri, and tetra deoxynucleotides. These were then extended by either stepwise or polymerization techniques to give longer chains of repeating di or tri nucleotide sequences that could be used to confirm the code.

Narang must have left Khorana in about 1967 to set up his own group in Ottawa. He has obviously been very productive since that time and it seems clear that he must have had considerable input into the previous work. In Canada he developed the phosphotriester method of polynucleotide synthesis into a very effective technique, which gives much better yields of much more homogeneous products. Although the principle was known even by Todd, the details had not been well worked out before. It required the discovery of new protecting groups, new phosphorylating reagents, new coupling reagents and new deprotection methods as well as the elaboration of improved separation techniques. I think it is the method of choice at this time. Narang also developed and applied the fragment condensation approach to repeating oligonucleotide synthesis, reaching at least to 24 residues.

In looking up some of Narang's papers I have realized that he is the one who synthesized the duplex DNA consisting of two 21-residue chains of the lac operon of E. coli. The synthetic product was shown to bind to the repressor protein. The duplex was also made by enzymatic repair synthesis and by ligase joining of shorter pieces, and in addition it was cloned. His group is now working on

the synthesis of the human insulin gene. He has made 8 oligo deoxyribonucleotides corresponding to the insulin A-chain and 17 purified fragments for the B-chain and mini C-chain. As far as I know their assembly is not yet complete, but it will be an impressive achievement when it is finished.

This technique has made possible the much publicized demonstration by Boyer's group of the first production of an active peptide hormone by cloning experiments. They synthesized the somatostatin gene by the triester method, fused it to the β-galactosidase gene on plasmid pBR322 and cloned it in E. coli. The synthetic work was carried out by Itakura, who was one of Narang's former associates. Zamecnik has also used the Narang method to make a tridecamer that will inhibit Rous Sarcoma Virus.

My impression is that Narang has done a substantial amount of very fine work in a difficult area and that he has made a substantial impact on the field. Both he and others have used his chemistry to carry out significant biological experiments. An honor such as the award of the Order of Canada appears to me to be well deserved.

Sincerely,

Bruce

Bruce Merrifield

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